

5

WHAT IS CLAIMED IS:

1. An isolated polynucleotide selected from the group consisting of:
- a) a nucleotide sequence comprising one or more polymorphic sequences (SEQ ID NOS:1 - 651);
 - b) a fragment of said nucleotide sequence, provided that the fragment includes a polymorphic site in said polymorphic sequence;
 - c) a complementary nucleotide sequence comprising a sequence complementary to one or more of said polymorphic sequences (SEQ ID NOS:1 - 651); and
 - d) a fragment of said complementary nucleotide sequence, provided that the fragment includes a polymorphic site in said polymorphic sequence.

2. The polynucleotide of claim 1, wherein said polynucleotide sequence is DNA.

3. The polynucleotide of claim 1, wherein said polynucleotide sequence is RNA.

4. The polynucleotide of claim 1, wherein said polynucleotide sequence is between about 10 and about 100 nucleotides in length.

5. The polynucleotide of claim 1, wherein said polynucleotide sequence is between about 10 and about 90 nucleotides in length.

5

6. The polynucleotide of claim 1, wherein said polynucleotide sequence is between about 10 and about 75 nucleotides in length.

10

7. The polynucleotide of claim 1, wherein said polynucleotide is between about 10 and about 50 bases in length.

8. The polynucleotide of claim 1, wherein said polynucleotide is between about 10 and about 40 bases in length.

15

9. The polynucleotide of claim 1, wherein said polynucleotide is derived from a nucleic acid encoding a polypeptide related to angiopoietin, 4-hydroxybutyrate dehydrogenase, ATP-dependent RNA helicase, MHC Class I histocompatibility antigen, or phosphoglycerate kinase.

20

10. The polynucleotide of claim 1, wherein said polymorphic site includes a nucleotide other than the nucleotide listed in Table 1, column 5 for said polymorphic sequence.

25

11. The polynucleotide of claim 1, wherein the complement of said polymorphic site includes a nucleotide other than the complement of the nucleotide listed in Table 1, column 5 for the complement of said polymorphic sequence.

- 5 12. The polynucleotide of claim 1, wherein said polymorphic site includes the
nucleotide listed in Table 1, column 6 for said polymorphic sequence.

SUB
A6

- 10 13. The polynucleotide of claim 1, wherein the complement of said polymorphic site
includes the complement of the nucleotide listed in Table 1, column 6 for said
polymorphic sequence.

14. An isolated allele-specific oligonucleotide that hybridizes to a first polynucleotide
at a polymorphic site encompassed therein, wherein the first polynucleotide is
chosen from the group consisting of:

SUB
A7

- 15 a) a nucleotide sequence comprising one or more polymorphic sequences
(SEQ ID NOS:1 - 651) provided that the polymorphic sequence
includes a nucleotide other than the nucleotide recited in Table 1,
column 5 for said polymorphic sequence;
- 20 b) a nucleotide sequence that is a fragment of said polymorphic sequence,
provided that the fragment includes a polymorphic site in said
polymorphic sequence;
- 25 c) a complementary nucleotide sequence comprising a sequence
complementary to one or more polymorphic sequences (SEQ ID NOS:1
- 651), provided that the complementary nucleotide sequence includes a
nucleotide other than the complement of the nucleotide recited in Table
1, column 5; and
- d) a nucleotide sequence that is a fragment of said complementary
sequence, provided that the fragment includes a polymorphic site in
said polymorphic sequence.

5 15. The oligonucleotide of claim 14, wherein the oligonucleotide does not hybridize under stringent conditions to a second polynucleotide selected from the group consisting of:

a) a nucleotide sequence comprising one or more polymorphic sequences (SEQ ID NOS:1 - 651), wherein said polymorphic sequence includes
10 the nucleotide listed in Table 1, column 5 for said polymorphic sequence;

b) a nucleotide sequence that is a fragment of any of said nucleotide sequences;

c) a complementary nucleotide sequence comprising a sequence
15 complementary to one or more polymorphic sequences (SEQ ID NOS:1 - 651), wherein said polymorphic sequence includes the complement of the nucleotide listed in Table 1, column 5; and

d) a nucleotide sequence that is a fragment of said complementary
20 sequence, provided that the fragment includes a polymorphic site in said polymorphic sequence.

16. The oligonucleotide of claim 15, wherein the oligonucleotide is between about 10 and about 51 bases in length.

25 17. The oligonucleotide of claim 15, wherein the oligonucleotide identifies a polypeptide related to angiopoietin, 4-hydroxybutyrate dehydrogenase, ATP-dependent RNA helicase, MHC Class I histocompatibility antigen, or phosphoglycerate kinase.

5 18. The oligonucleotide of claim 15, wherein the oligonucleotide is between about 15 and about 30 bases in length.

19/ A method of detecting a polymorphic site in a nucleic acid, the method comprising:

10 a) contacting said nucleic acid with an oligonucleotide that hybridizes to a polymorphic sequence selected from the group consisting of SEQ ID NOS: 1 - 651, or its complement, provided that the polymorphic sequence includes a nucleotide other than the nucleotide recited in Table 1, column 5 for said polymorphic sequence, or the complement includes a nucleotide other than the complement of the nucleotide recited in Table 1, column 5; and

b) determining whether said nucleic acid and said oligonucleotide hybridize;

whereby hybridization of said oligonucleotide to said nucleic acid sequence indicates the presence of the polymorphic site in said nucleic acid.

20. The method of claim 19, wherein said oligonucleotide does not hybridize to said polymorphic sequence when said polymorphic sequence includes the nucleotide recited in Table 1, column 5 for said polymorphic sequence, or when the complement of the polymorphic sequence includes the complement of the nucleotide recited in Table 1, column 5 for said polymorphic sequence.

21. The method of claim 19, wherein said oligonucleotide identifies a polypeptide related to angiopoietin, 4-hydroxybutyrate dehydrogenase, ATP-dependent RNA helicase, MHC Class I histocompatibility antigen, or phosphoglycerate kinase.

5

22. The method of claim 19, wherein said oligonucleotide is between about 15 and about 30 bases in length.

10 ~~23.~~ A method of detecting the presence of a sequence polymorphism in a subject, the method comprising:

a) providing a nucleic acid from said subject;

b) contacting said nucleic acid with an oligonucleotide that hybridizes to a polymorphic sequence selected from the group consisting of SEQ ID NOS:1 - 651, or its complement, provided that the polymorphic sequence includes a nucleotide other than the nucleotide recited in for
15 said polymorphic sequence, or the complement includes a nucleotide other than the complement of the nucleotide recited in Table 1, column 5; and

c) determining whether said nucleic acid and said oligonucleotide
20 hybridize;

whereby hybridization of said oligonucleotide to said nucleic acid sequence indicates the presence of the polymorphism in said subject.

25 ~~24.~~ A method of determining the relatedness of a first and second nucleic acid, the method comprising:

a) providing a first nucleic acid and a second nucleic acid;

b) contacting said first nucleic acid and said second nucleic acid with an oligonucleotide that hybridizes to a polymorphic sequence selected from the group consisting of SEQ ID NOS:1 - 651, or its complement,

5 provided that the polymorphic sequence includes a nucleotide other than the nucleotide recited in Table 1, column 5 for said polymorphic sequence, or the complement includes a nucleotide other than the complement of the nucleotide recited in Table 1, column 5;

10 c) determining whether said first nucleic acid and said second nucleic acid hybridize to said oligonucleotide; and

d) comparing hybridization of said first and second nucleic acids to said oligonucleotide,

wherein hybridization of the first and second nucleic acids to said oligonucleotide indicates the first and second nucleic acids are related.

15

25. The method of claim 24, wherein said oligonucleotide does not hybridize to said polymorphic sequence when said polymorphic sequence includes the nucleotide recited in Table 1, column 5 for said polymorphic sequence, or when the complement of the polymorphic sequence includes the complement of the nucleotide recited in Table 1, column 5 for said polymorphic sequence.

20

26. The method of claim 24, wherein the oligonucleotide is between about 10 and about 51 bases in length.

25

27. The method of claim 24, wherein the oligonucleotide is between about 10 and about 40 bases in length.

28. The method of claim 24, wherein the oligonucleotide is between about 15 and about 30 bases in length.

5 ~~29.~~ An isolated polypeptide comprising a polymorphic site at one or more amino acid
residues, wherein the protein is encoded by a polynucleotide selected from the
group consisting of: polymorphic sequences SEQ ID NOS:1 - 651, or their
complement, provided that the polymorphic sequence includes a nucleotide other
than the nucleotide recited in Table 1, column 5 for said polymorphic sequence,
10 or the complement includes a nucleotide other than the complement of the
nucleotide recited in Table 1, column 5.

15 30. The polypeptide of claim 29, wherein said polypeptide is translated in the same
open reading frame as is a wild type protein whose amino acid sequence is
identical to the amino acid sequence of the polymorphic protein except at the site
of the polymorphism.

20 31. The polypeptide of claim 29, wherein the polypeptide encoded by said
polymorphic sequence, or its complement, includes the nucleotide listed in Table
2, column 6 or Table 3, column 5 for said polymorphic sequence, or the
complement includes the complement of the nucleotide listed in Table 1, column
6.

25 ~~32.~~ An antibody that binds specifically to a polypeptide encoded by a polynucleotide
comprising a nucleotide sequence encoded by a polynucleotide selected from the
group consisting of polymorphic sequences SEQ ID NOS:1 - 651, or its
complement, provided that the polymorphic sequence includes a nucleotide other
than the nucleotide recited in Table 1, column 5 for said polymorphic sequence,
or the complement includes a nucleotide other than the complement of the
30 nucleotide recited in Table 1, column 5.

5 33. The antibody of claim 32, wherein said antibody binds specifically to a polypeptide encoded by a polymorphic sequence which includes the nucleotide listed in Table 1, column 6 for said polymorphic sequence.

10 34. The antibody of claim 32, wherein said antibody does not bind specifically to a polypeptide encoded by a polymorphic sequence which includes the nucleotide listed in Table 1, column 5 for said polymorphic sequence.

35. A method of detecting the presence of a polypeptide having one or more amino acid residue polymorphisms in a subject, the method comprising

- 15 a) providing a protein sample from said subject;
- b) contacting said sample with the antibody of claim 34 under conditions that allow for the formation of antibody-antigen complexes; and
- c) detecting said antibody-antigen complexes,

20 whereby the presence of said complexes indicates the presence of said polypeptide.

36. A method of treating a subject suffering from, at risk for, or suspected of, suffering from a pathology ascribed to the presence of a sequence polymorphism in a subject, the method comprising:

- 25 a) providing a subject suffering from a pathology associated with aberrant expression of a first nucleic acid comprising a polymorphic sequence selected from the group consisting of SEQ ID NOS:1 - 651, or its complement; and

- 5 b) administering to the subject an effective therapeutic dose of a second nucleic acid comprising the polymorphic sequence, provided that the second nucleic acid comprises the nucleotide present in a wild type allele of the sequence polymorphism,

thereby treating said subject.

10

37. The method of claim 36, wherein the second nucleic acid sequence comprises a polymorphic sequence which includes the nucleotide listed in Table 1, column 5 for said polymorphic sequence.

15

38. A method of treating a subject suffering from, at risk for, or suspected of suffering from a pathology ascribed to the presence of a sequence polymorphism in a subject, the method comprising:

20

- a) providing a subject suffering from a pathology associated with aberrant expression of a polymorphic sequence selected from the group consisting of polymorphic sequences SEQ ID NOS:1 - 651, or its complement; and

25

- b) administering to the subject an effective therapeutic dose of a polypeptide,
- wherein said polypeptide is encoded by a polynucleotide comprising a polymorphic sequence selected from the group consisting of SEQ ID NOS:1 - 651, or by a polynucleotide comprising a nucleotide sequence that is complementary to any one of polymorphic sequences SEQ ID NOS:1 - 651, provided that said polymorphic sequence includes the nucleotide listed in Table 1, column 6 for said polymorphic sequence, thereby treating said subject.

30

5 ~~39.~~ A method of treating a subject suffering from, at risk for, or suspected of suffering from, a pathology ascribed to the presence of a sequence polymorphism in a subject, the method comprising:

a) providing a subject suffering from, at risk for, or suspected of suffering from, a pathology associated with aberrant expression of a first nucleic acid comprising a polymorphic sequence selected from the group consisting of SEQ ID NOS:1 - 651, or its complement; and

b) administering to the subject an effective dose of the antibody of claim

34,

thereby treating said subject.

15 ~~40.~~ A method of treating a subject suffering from, at risk for, or suspected of suffering from, a pathology ascribed to the presence of a sequence polymorphism in a subject, the method comprising:

a) providing a subject suffering from, at risk for, or suspected of suffering from, a pathology associated with aberrant expression of a nucleic acid comprising a polymorphic sequence selected from the group consisting of SEQ ID NOS:1 - 651, or its complement; and

b) administering to the subject an effective dose of an oligonucleotide comprising a polymorphic sequence selected from the group consisting of SEQ ID NOS:1 - 651, or by a polynucleotide comprising a nucleotide sequence that is complementary to any one of polymorphic sequences SEQ ID NOS:1 - 651, provided that said polymorphic sequence includes the nucleotide listed in Table 1, column 6 for said polymorphic sequence,

thereby treating said subject.

5

41. An oligonucleotide array, comprising one or more oligonucleotides hybridizing to a first polynucleotide at a polymorphic site encompassed therein, wherein the first polynucleotide is chosen from the group consisting of:

- 10 a) a nucleotide sequence comprising one or more polymorphic sequences
SEQ ID NOS:1 - 651;
- b) a nucleotide sequence that is a fragment of any of said nucleotide
sequence, provided that the fragment includes a polymorphic site in
said polymorphic sequence;
- 15 c) a complementary nucleotide sequence comprising a sequence
complementary to one or more polymorphic sequences SEQ ID NOS:1
- 651; and
- d) a nucleotide sequence that is a fragment of said complementary
sequence, provided that the fragment includes a polymorphic site in
said polymorphic sequence.
- 20

42. The array of claim 41, wherein said array comprises 10 oligonucleotides.

43. The array of claim 41, wherein said array comprises at least 100 oligonucleotides.

25 44. The array of claim 41, wherein said array comprises at least 1000
oligonucleotides.

Added
178